EDITORIAL

B-type natriuretic peptide: a role in selection and follow up of the implantable cardioverter-defibrillator patient?

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B-type natriuretic peptide may have a role in predicting the risk of ICD therapy, identifying patients with deteriorating clinical status and allowing them to be selected for more detailed medical review and, if necessary, drug treatment

B-type natriuretic peptide (BNP) is a member of a group of structurally related hormones, the natriuretic peptides. The group includes atrial natriuretic peptide (ANP) and C-type natriuretic peptide (CNP). At physiological concentrations these three peptides play a complex role in body fluid homeostasis and vascular tone. In humans, BNP is predominantly secreted from the ventricles. It has a half life of 15–20 minutes and can be secreted rapidly in response to acute volume overload.

BNP can be measured using laboratory based or bedside radioimmunoassay methods. Potential clinical utility for BNP measurement has been demonstrated for a number of roles including exclusion of heart failure in primary care, acute diagnosis of heart failure in hospital, as a marker of prognosis following myocardial infarction and acute coronary syndromes, and for monitoring of patients with chronic heart failure. BNP values can also predict the risk of sudden cardiac death in patients with impaired left ventricular function.[1]

BNP IN ICD PATIENTS

In this issue of *Heart*, Verma and colleagues[2] report on the utility of BNP measurements taken on the day before implantable cardioverter-defibrillator (ICD) implantation in 345 patients, 52% of whom were receiving an ICD for primary prevention. Patients with previous ICD implants and patients receiving a biventricular ICD were excluded. Over an average 13 month follow up, 18% of patients received appropriate ICD therapy. Univariate analysis showed appropriate ICD therapy to be associated with lower ejection fraction, non-use of amiodarone, and higher BNP concentrations. BNP values were divided into quartiles and the relative risk of appropriate ICD therapy in each quartile was 1.0/4.74/5.83/8.72. Cox multivariate regression analysis was performed looking at age, sex, ICD indication, left ventricular (LV) function, coronary artery disease (CAD), non-ischaemic cardiomyopathy (NICM), congestive heart failure (CHF) history, advanced New York Heart Association (NYHA) class (III or IV), β blocker use, amiodarone use, plasma BNP concentration, and plasma C reactive protein (CRP) concentration. Only BNP emerged as a significant predictor of appropriate ICD therapy, suggesting that BNP could be the most powerful identifier of arrhythmic risk. However, this finding may have been influenced by the authors' choice to compare BNP as a dichotomised variable (greater or less than the 50th centile) versus left ventricular ejection fraction (LVEF) divided in 5% steps. Nonetheless, BNP concentration measured before ICD implant is clearly capable of identifying those at greater risk of arrhythmia occurrence over the first year after ICD implantation. By contrast CRP concentrations, also examined in this study, were not predictive of subsequent appropriate ICD therapy.

BNP AS A TOOL FOR THE SELECTION OF ICD PATIENTS?

Because of its predictive value for future risk of sudden arrhythmic death, LVEF has been extensively used as a principle selection criterion in the clinical trials of ICD use for primary and secondary prevention. Major clinical trials such as MADIT-II[3] and SCD-Heft[4] have shown that such a strategy can identify patients who benefit from prophylactic implantation of an ICD. The findings from these trials have been incorporated into current clinical and practice guidelines.[5 6] In general the ICD trials have accepted patients with LVEF measurements obtained from echocardiography, coronary angiography, or radionuclide scans.

However, there are significant limitations in the ability of LVEF to identify patients at high risk of sudden cardiac death. These are due to less than perfect repeatability in measurement, whether by echocardiography, angiography, or radionuclide angiography and also to the difficulty of using a single threshold value of a continuous variable to separate low and high risk.[7] Although more than one assay exists for BNP values, it is possible that standardisation on a single assay method and threshold value might allow a more consistent and repeatable approach to selection of patients for ICD therapy and that the BNP measurement might inherently contain more information about subsequent risk than ejection fraction alone. This remains to be proven.

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Abbreviations: ANP, atrial natriuretic peptide; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CHF, congestive heart failure; CNP, C-type natriuretic peptide; ICD, implantable cardioverter-defibrillator; LV, left ventricular; LVEF, left ventricular ejection fraction; NICM, non-ischaemic cardiomyopathy; NYHA, New York Heart Association

Validation of BNP as a selection criterion for ICD implantation would require studies of large numbers of patients being considered for ICD implantation using conventional selection criteria. In parallel with BNP measurement in patients receiving an ICD, there would be a requirement for a registry of patients who failed to meet existing criteria for ICD implantation in whom BNP would also be measured. Follow up for at least 2–3 years would be required to see whether a cut off value for BNP could be identified which would perform at least as well as conventional ejection fraction thresholds in identifying patients whose mortality would be reduced by ICD implantation. Given the relative ease with which BNP measurement can be repeated in comparison with measurement of ejection fraction, there might also be a role for multiple measurements of BNP.

BNP AS A TOOL FOR THE FOLLOW UP OF ICD PATIENTS

The steady increase in ICD implantation rates coupled with excellent long term survival in ICD recipients is resulting in substantial growth in the number of ICD patients in follow up. Given the current shortage of clinical physiologists (cardiac technicians) and specialist electrophysiologists in the UK, delivery of high quality follow up services is a challenge. In many centres ICD follow up clinics are clinical physiologist led; with the increasing chronicity of many ICD implants there is a need to ensure that changes in the underlying cardiac condition of the patient are not overlooked.

Current selection criteria ensure that many patients receiving ICDs either have heart failure or are at risk of developing it. Regular measurement of BNP in the clinic could allow the identification of patients who were at risk of deteriorating clinical status and allow them to be selected for more detailed medical review and subsequent adjustment of drug treatment. BNP measurement has also been shown to be a useful marker of response to biventricular pacing,[8] a therapy which is increasingly being combined with ICD use.

Being able to predict the risk of ICD therapy delivery over the next 6–12 months would be very useful. Frequent ICD therapies can have an adverse psychological impact, result in loss of social privileges such as driving, and can impact on the longevity of the ICD. Identification of an increased risk of therapy could be used to target antiarrhythmic drug treatments to reduce the risk of subsequent ICD therapy.[9]

In summary, the link between BNP values and subsequent appropriate therapy delivery highlighted by Verma and colleagues[2] is one which deserves further exploration as we strive to provide ICD implantation targeted to those at greatest risk, and to ensure that standards are maintained as the population in the device follow up clinic grows.

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